Management of Type 2 Diabetes: Putting the 2020 Guidelines into Practice

Presented as a Live Webinar

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FACULTY

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WEBINAR INFORMATION

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Management of Type 2 Diabetes: Putting the 2020 Guidelines into Practice

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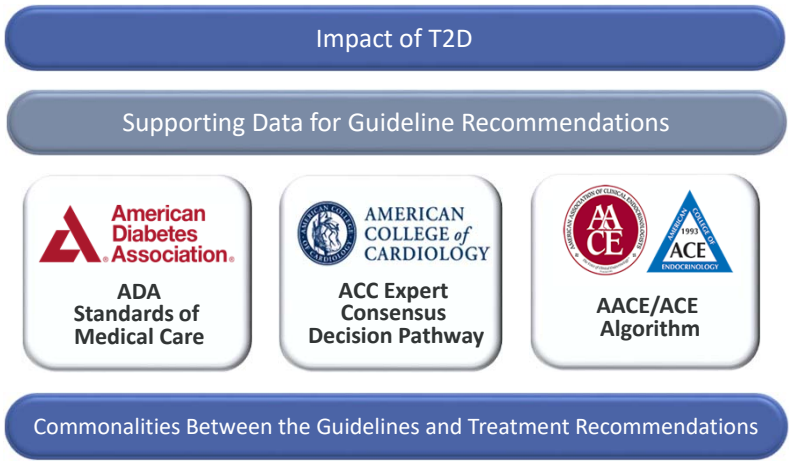
Learning Objectives

At the conclusion of this educational activity, participants should be able to

- Describe evidence from recent landmark CVOTs used to support guideline recommendations for the management of T2D.
- Identify commonalities among national guidelines and recommended treatment pathways based on CV risk assessment of patients with T2D.
- Recognize the need to manage cardiovascular disease and risk factors within the paradigm of the overall management of T2D.

CVOTs = cardiovascular outcome trials ; T2D = type 2 diabetes; CV = cardiovascular

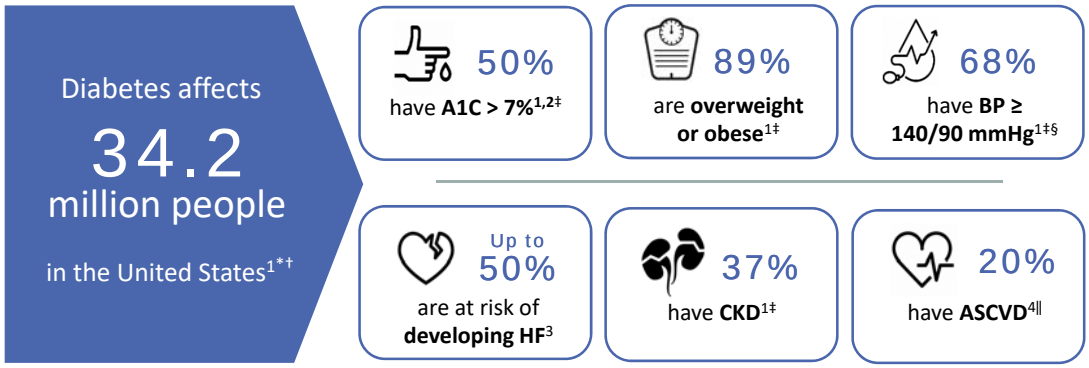
Content Overview



AACE = American Association of Clinical Endocrinologists; ACE = American College of Endocrinology; ACC = American College of Cardiology; ADA = American Diabetes Association

Impact of T2D

T2D is Associated with Multiple Comorbid Conditions



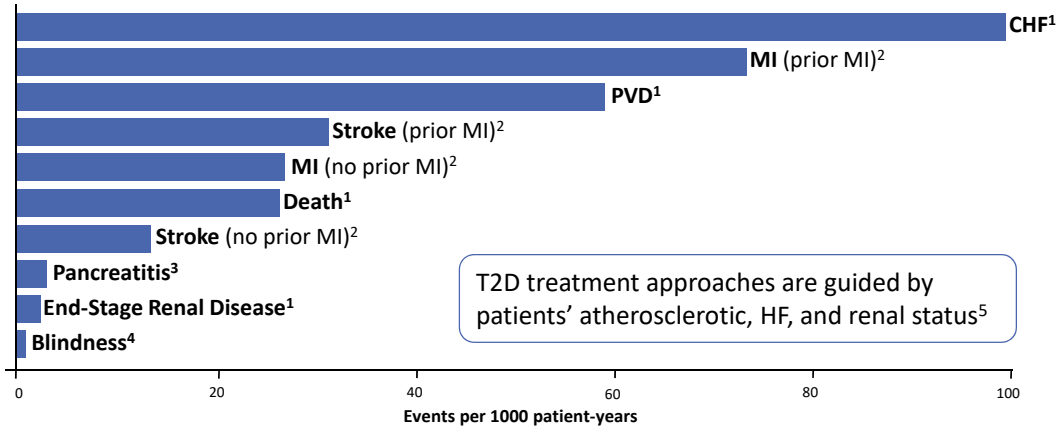
*All ages, 2018. †90%–95% of diabetes represents type 2 diabetes. ‡Adults 18 years or older with a diagnosis of diabetes in the United States, 2013–2016. §Or taking antihypertensive medications. ‖Defined as myocardial infarction, ischemic heart disease, peripheral arterial disease, or cerebrovascular disease.

A1C = glycated hemoglobin; ASCVD = atherosclerotic cardiovascular disease; BP = blood pressure; CKD = chronic kidney disease; HF = heart failure

1. CDC. National Diabetes Statistics Report. 2020. Accessed February 19, 2020. 2. Carls G et al. *Diabetes Ther*. 2017;8:863-73. 3. American Diabetes Association. Standards of Medical Care in Diabetes 2020. *Diabetes Care*. 2020;43(supplement 1):S1-S212. 4. Iglay K et al. *Curr Med Res Opin*. 2016;32:1243-52.

Common Complications in Patients With Type 2 Diabetes

Excess Risk of Events in Patients With Diabetes Relative to Patients Without Diabetes

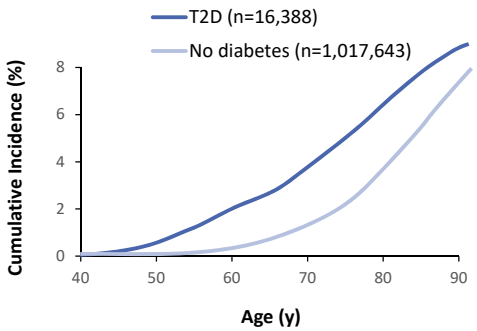


T2D treatment approaches are guided by patients' atherosclerotic, HF, and renal status[5]

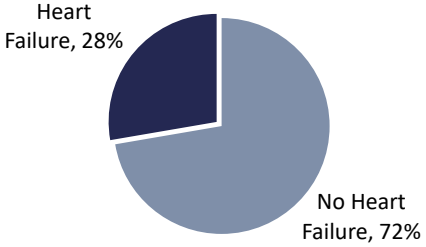
Adapted from Bergenstal RM et al. *Am J Med*. 2010;123:374.e 9-18.
CHF = congestive heart failure; HF = heart failure; MI = myocardial infarction; PVD = peripheral vascular disease
1. Foley RN et al. *J Am Soc Nephrol*. 2005;16:489-95. 2. Haffner SM et al. *N Engl J Med*. 1998;339:229-34. 3. Noel RA et al. *Diabetes Care*. 2009;32:834-8.
4. Trautner C et al. *Diabetes Care*. 1997;20:1147-53. 5. Garber AJ et al. *Endocr Pract*. 2020;26:107-39.

HF Develops Earlier in Patients with T2D than in Those Without T2D and is Frequently Underdiagnosed

HF Incidence by Age Range[1]



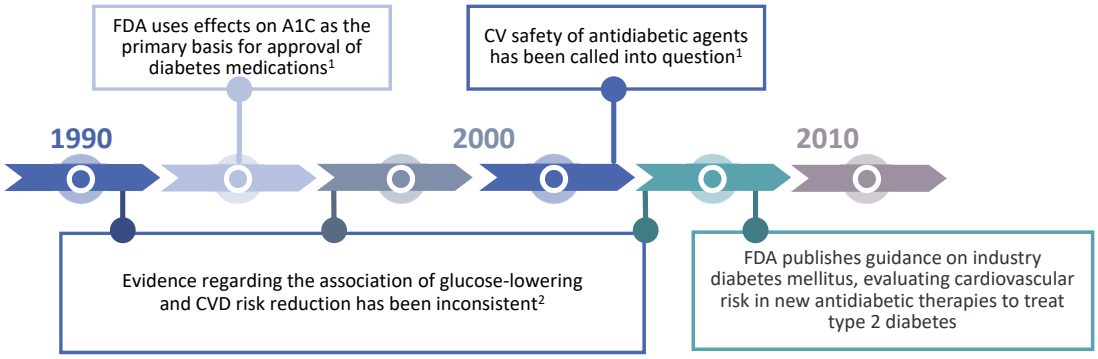
Patients with Type 2 Diabetes Previously Undiagnosed with HF[2,a] (n=581)



[a]Patients with T2D aged ≥60 years without known HF underwent a standardized diagnostic workup, including medical history, physical examination, electrocardiogram, and echocardiography.
1. Shah AD, et al. *Lancet Diabetes Endocrinol.* 2015;3(2):105-113. 2. Boonman-de Winter LJM, et al. *Diabetologia*. 2012;55(8):2154-2162.

Supporting Data for Guideline Recommendations

History of CV Safety with Antidiabetic Agents and FDA Guidance



The 2008 FDA Guidance for Industry recommends pre-approval and post-approval CV assessment for drugs and biologics for the treatment of type 2 diabetes[1]

A1C = glycated hemoglobin; CV = cardiovascular; CVD = cardiovascular disease; FDA = Food and Drug Administration

1. Joffe HV et al. *Rev Endocr Metab Disord*. 2010;11:21-30. 2. Hirshberg B et al. *Diabetes Care*. 2011;34(suppl 2):S101-106.

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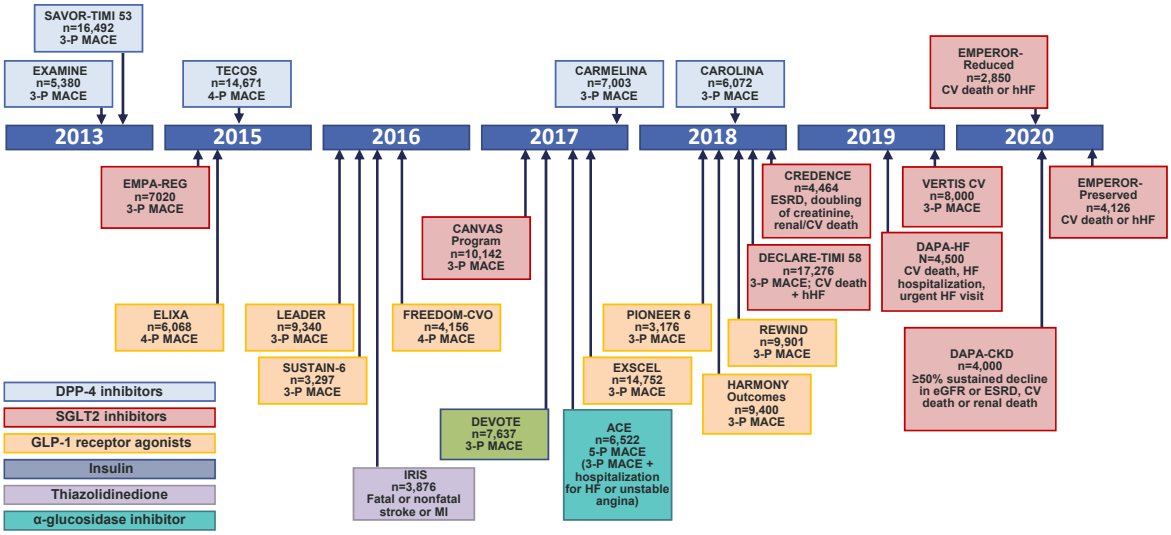
Trials to Assess Newer Glucose Lowering Therapies for CV Outcomes



ACE = acetylcholine esterase; CKD = chronic kidney disease; DPP-4 = dipeptidyl peptidase-4; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; GLP-1 = glucagon-like peptide 1; HF = heart failure; MACE = major adverse cardiovascular events; MI = myocardial infarction; SGLT2 = sodium glucose cotransporter 2

Cefalu WT et al. *Diabetes Care.* 2018;41:14-31.

Can we directly compare CV results across CVOTs if the FDA okays the design of the trial?

a. We can, and we should
b. We cannot as the FDA approval process is too complex
c. We can as long as we account for duration of the trial as per FDA
d. We cannot as the baseline characteristics and designs are different despite FDA's input

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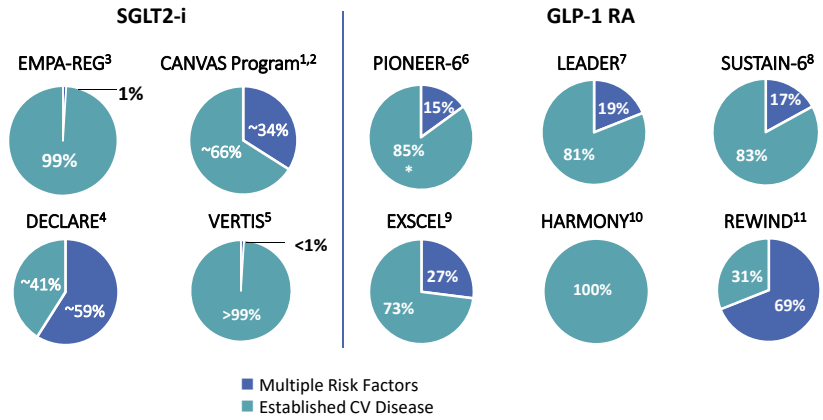
Cardiovascular Outcomes Trials: Percentage of Patients with and without CVD



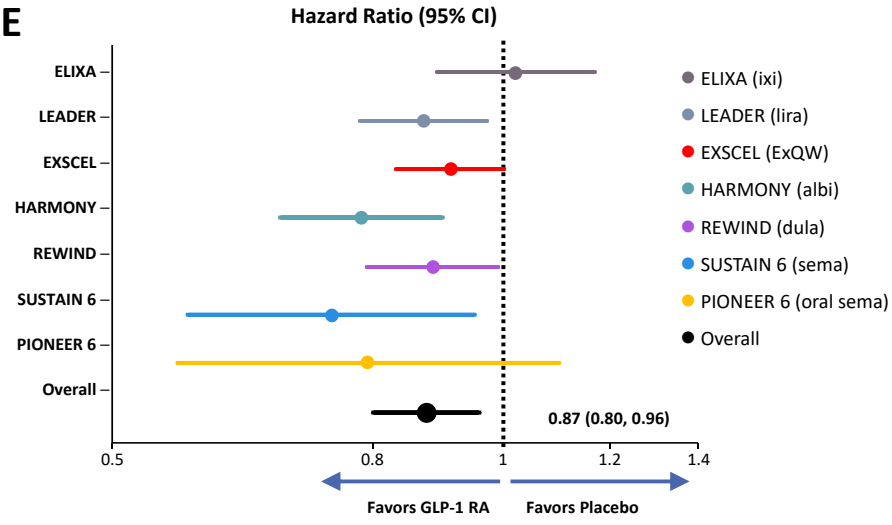
In the general T2D population, only 20% of patients have established CVD[12]

*PIONEER-6 inclusion criteria were the age of ≥50 years with established cardiovascular or chronic kidney disease. CREDENCE (canagliflozin) not included due to makeup of the study population which included patients with T2D and diabetic nephropathy with albuminuria >300 mg/day.

CV = cardiovascular; CVD = cardiovascular disease; GLP-1 = glucagon-like peptide 1; RA = receptor agonist; SGLT2-i = sodium glucose cotransporter 2 inhibitor

1. Neal B et al. *N Engl J Med*. 2017;377:644-57. 2. Neal B et al. *Diabetes Obes Metab*. 2017;19:926-35. 3. Zinman B et al. *N Engl J Med*. 2015;373:2117-28; 4. Wiviott SD et al. *N Engl J Med*. 2019;380:347-57. 5. Cannon CP et al. *Am Heart J*. 2018;206:11-23. 6. Husain M et al. *N Engl J Med*. 2019;381:841-51. 7. Marso SP et al. *N Engl J Med*. 2016;375:311-22. 8. Marso SP et al. *N Engl J Med*. 2016;375:1834-44. 9. Holman RR et al. *N Engl J Med*. 2017;377:1228-39. 10. Hernandez AF et al. *Lancet*. 2018;392(10157):1519-29. 11. Gerstein HC et al. *Diabetes Obes Metab*. 2017;1-8. 12. Iglay K et al. Curr *Med Res Opin*. 2016;32:1243-52.

GLP-1 RA MACE Overview

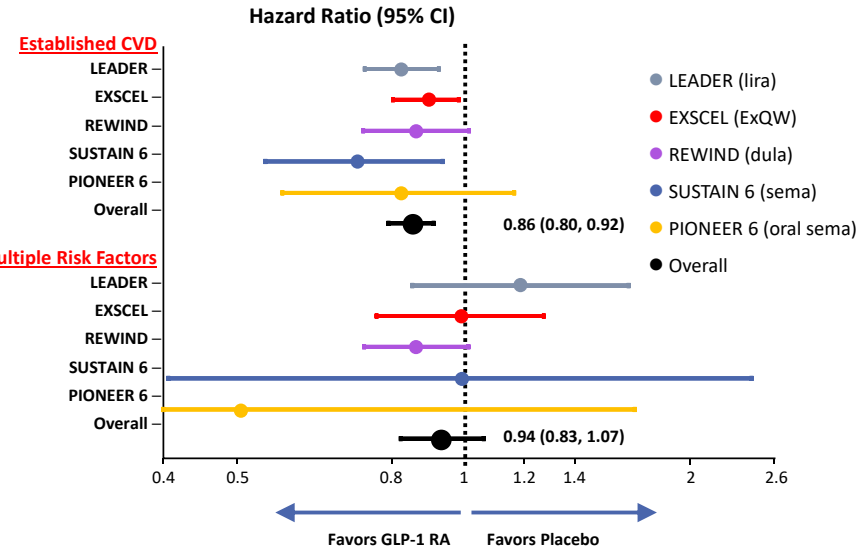


CI = confidence interval; GLP-1 – glucagon-like peptide 1; MACE = major adverse cardiovascular event; RA = receptor agonist

Giugliano D et al. *Diabet Obes Metab.* 2019;21:2576-80. doi: 10.1111/dom.13847.

GLP-1 RA MACE Overview:

Established CVD or Multiple Risk Factors

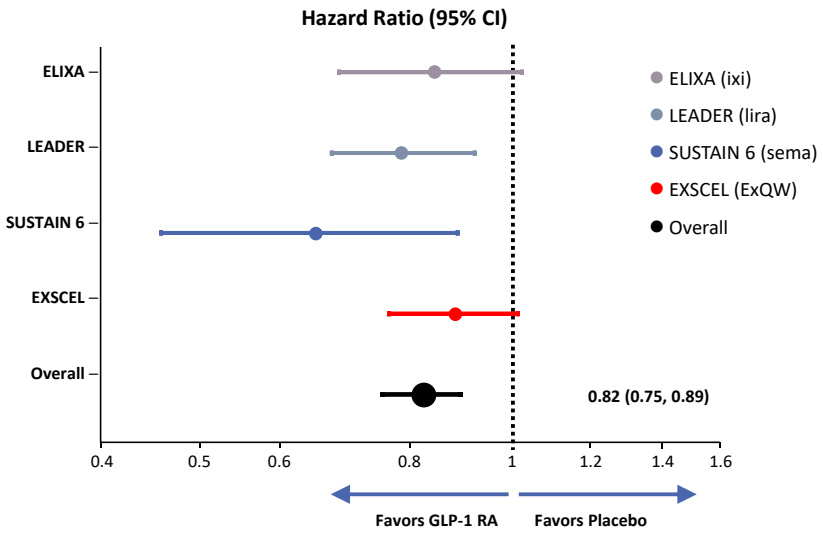


CI = confidence interval; CVD = cardiovascular disease; GLP-1 = glucagon-like peptide-1; RA = receptor agonist

Giugliano D et al. *Diabet Obes Metab.* 2019;21:2576-80. doi: 10.1111/dom.13847.

GLP-1 RA Renal Composite Overview:

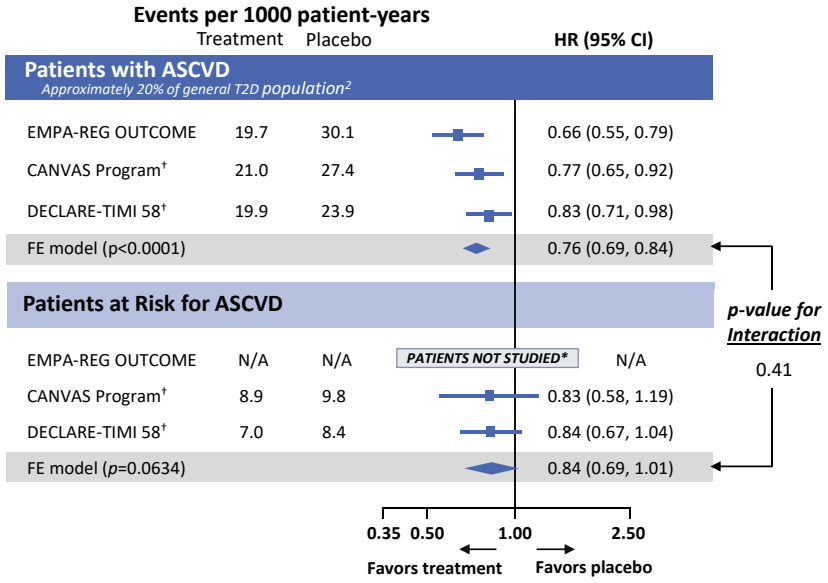
New-onset macroalbuminuria, sustained doubling of serum creatinine, or a 40% decline in eGFR, end-stage kidney disease, or death of renal cause



CI = confidence interval; eGFR = estimated glomerular filtration rate; GLP-1 = glucagon-like peptide-1; RA = receptor agonist

Adapted from Zelniker TA et al. *Circulation*. 2019;139:2022-31.

Meta-Analyses of T2D Treatments: SGLT2 Inhibitors on MACE[1‡]



*More than 99% of patients had established cardiovascular disease.[3]

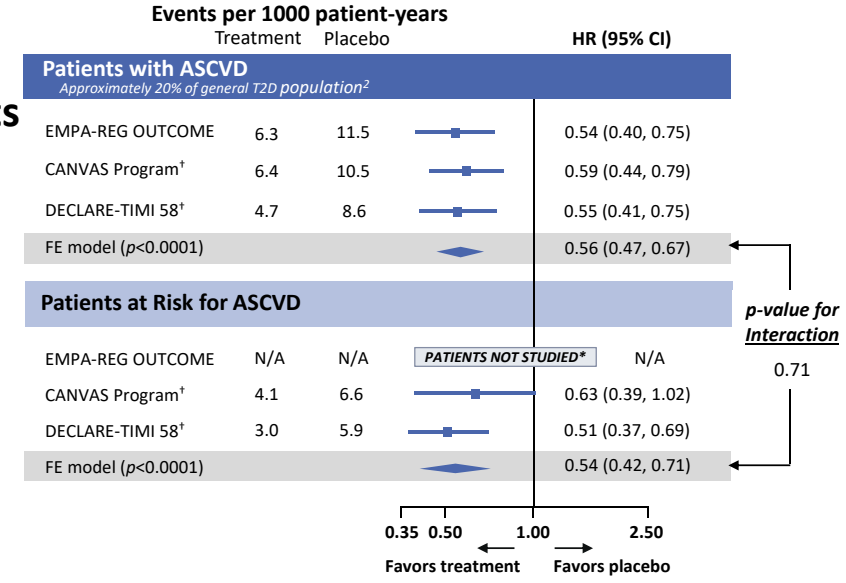
†Not powered to assess individual subgroups with or without ASCVD.

‡Results for VERTIS-CV (ertugliflozin; HR 0.99; 95% CI; 0.88-1.12) in T2D patients with established CVD and CREDENCE (canagliflozin; HR 0.85; 95% CI; 0.69-1.06) in T2D patients with diabetic nephropathy and albuminuria >300 mg/day were not available at the time of publication.

ASCVD = atherosclerotic cardiovascular disease; CI = confidence interval; FE = fixed effects; HR = hazard ratio; MACE = major adverse cardiovascular event; N/A = not applicable; SGLT2 = sodium glucose cotransporter-2

1. Adapted from Zelniker TA et al. *Lancet*. 2019;393(10166):31-9. 2. Iglay K et al. *Curr Med Res Opin*. 2016;32:1243-52. 3. Zinman B et al. *N Engl J Med*. 2015;373:2117-28.

Meta-Analyses of T2D Treatments in the US: SGLT2 Inhibitors on Renal Composite Data[1‡]



Renal composite of worsening eGFR, end-stage renal disease, or renal death.

*More than 99% of patients had established cardiovascular disease.[3]

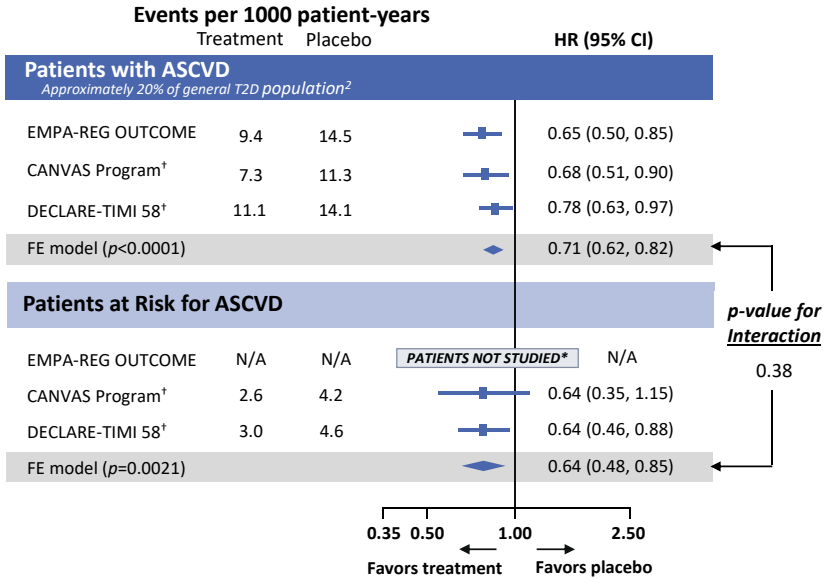
†Not powered to assess individual subgroups with or without ASCVD.

‡Results for VERTIS-CV (ertugliflozin; HR 0.66; 95% CI; 0.53-0.81) in T2D patients with established ASCVD and CREDENCE (canagliflozin; HR 0.85; 95% CI; 0.64-1.03) in T2D patients with diabetic nephropathy and albuminuria >300 mg/day were not available at the time of publication.

ASCVD = atherosclerotic cardiovascular disease; CI = confidence interval; FE = fixed effects; HR = hazard ratio; N/A = not applicable; SGLT2 = sodium glucose cotransporter-2

1. Adapted from Zelniker TA et al. *Lancet*. 2019;393(10166):31-9. 2. Iglay K et al. *Curr Med Res Opin*. 2016;32:1243-52. 3. Zinman B et al. *N Engl J Med*. 2015;373:2117-28.

Meta-Analyses of T2D Treatments in the US: SGLT2 Inhibitors on hHF[1‡]



*More than 99% of patients had established cardiovascular disease.[3]

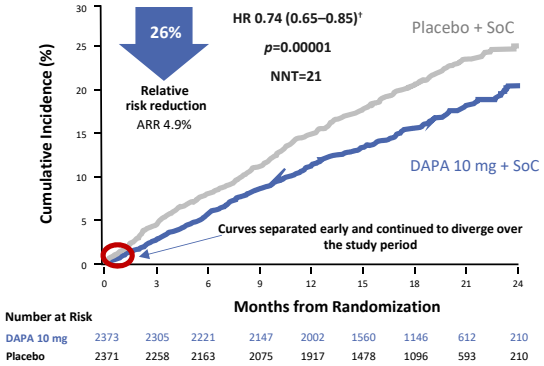
†Not powered to assess individual subgroups with or without ASCVD.

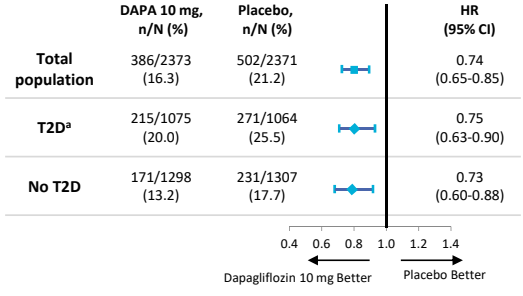
‡Results for VERTIS-CV (ertugliflozin; HR 0.7; 95% CI; 0.54-0.90) in T2D patients with established ASCVD and CREDENCE (canagliflozin; HR 0.61; 95% CI; 0.44-0.85) in T2D patients with diabetic nephropathy and albuminuria >300 mg/day were not available at the time of publication.

ASCVD = atherosclerotic cardiovascular disease; CI = confidence interval; FE = fixed effects; hHF = hospitalization for heart failure; HR = hazard ratio; N/A = not applicable; SGLT2 = sodium glucose cotransporter 2

1. Adapted from Zelniker TA et al. *Lancet*. 2019;393(10166):31-9. 2. Iglay K et al. *Curr Med Res Opin*. 2016;32:1243-52. 3. Zinman B et al. *N Engl J Med*. 2015;373:2117-28.

Dapagliflozin[a] Significantly Reduced the Relative Risk of the Primary Endpoint, CV Death, or Hospitalization for HF*, Regardless of Baseline Glycemic Status[1-3]





Dapagliflozin is now recommended (Level A) by the ADA 2020 Standards of Medical Care based on the findings from DAPA-HF

*Includes urgent HF visit requiring intravenous therapy. †Data represented as event rates over a median follow-up of 18.2 months.[1] [a]Dapagliflozin is approved in patients with HFrEF with and without T2D. §A non-significant result for an interaction test can be interpreted as the consistency of effect across the subgroup.[4]

ADA = American Diabetes Association; ARR = absolute risk reduction; ; CI = confidence interval; DAPA = dapagliflozin; HF = heart failure; HFrEF = heart failure with a reduced ejection fraction; HR = hazard ratio; NNT = number needed to treat; SoC = standard of care

1. McMurray JJV et al. *N Engl J Med*. 2019;381:1995-2008. 2. Petrie MC et al. *JAMA*. 2020;323:1353-68. 3. FARXIGA® (dapagliflozin) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; May 2020. 4. Alosh M et al. *J Biopharm Stat*. 2015;25:1161-78.

In national T2D algorithms, if a patient has an uncontrolled A1C (<1% to goal), no history of CVD or CKD, what is the first recommended oral therapy?

a. An SGLT2 inhibitor
b. A GLP-1 receptor agonist
c. Metformin
d. A sulfonylurea

ADA Standards of Medical Care

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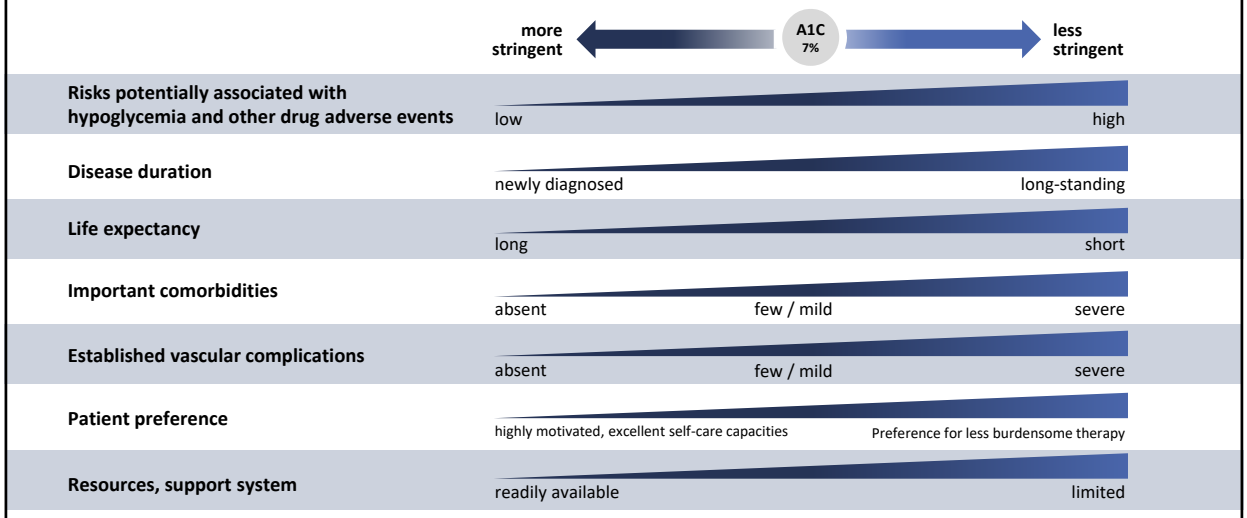
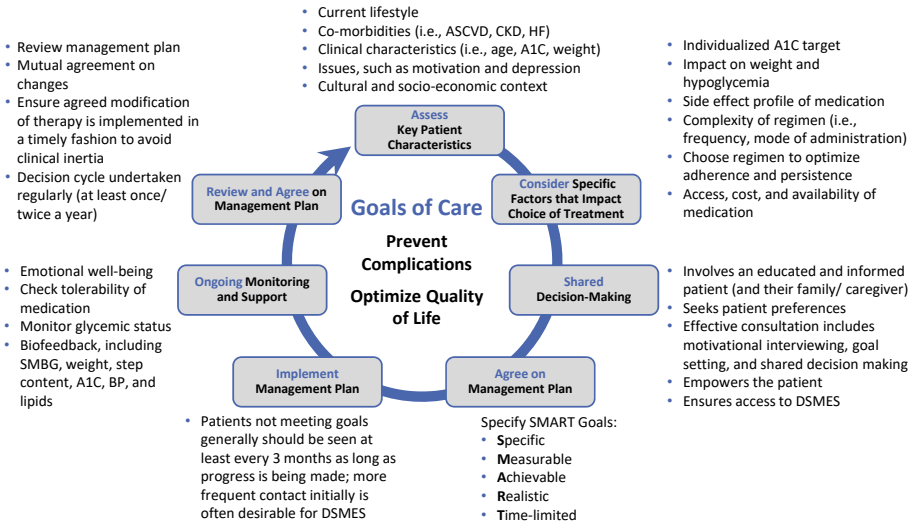
ADA Approach to Selection of Glycemic Target



A1C = glycated hemoglobin; ADA = American Diabetes Association

American Diabetes Association. Standards of Medical Care in Diabetes 2020. *Diabetes Care.* 2020;43(supplement 1):S1-S212.

2020 ADA Standards of Medical Care: Decision Cycle for Patient-Centered Glycemic Management



Adapted from American Diabetes Association. Standards of Medical Care in Diabetes—2019. *Diabetes Care*. 2019;42(Supplement 1):S35.

A1C = glycosylated hemoglobin; ADA = American Diabetes Association; ASCVD = atherosclerotic cardiovascular disease; BP = blood pressure; CKD = chronic kidney disease; DSMES = diabetes self-management education and support; SMBG = self-monitored blood glucose.

American Diabetes Association. Standards of Medical Care in Diabetes 2020. *Diabetes Care*. 2020;43(supplement 1):S1-S212.

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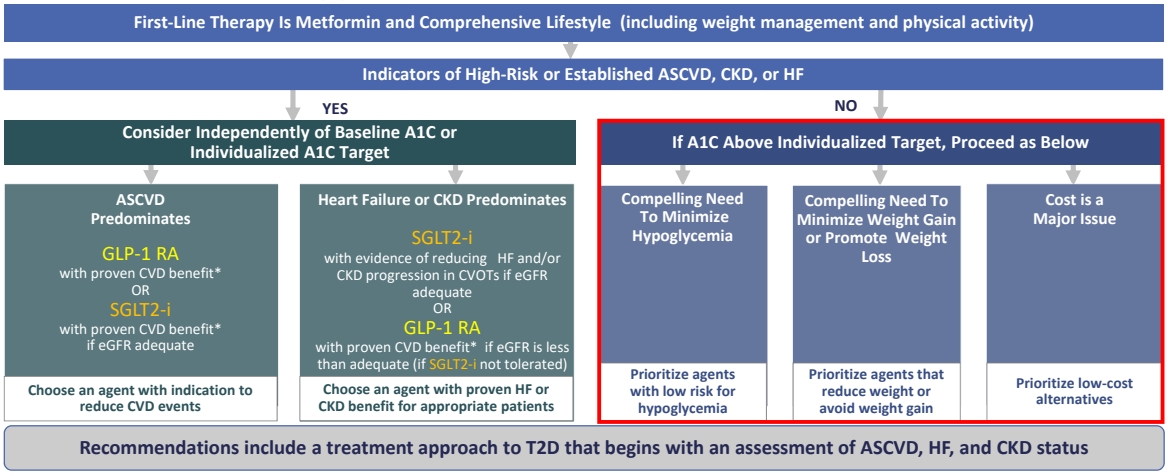
2020 ADA Standards of Medical Care Antihyperglycemic Medication in Type 2 Diabetes: Overall Approach

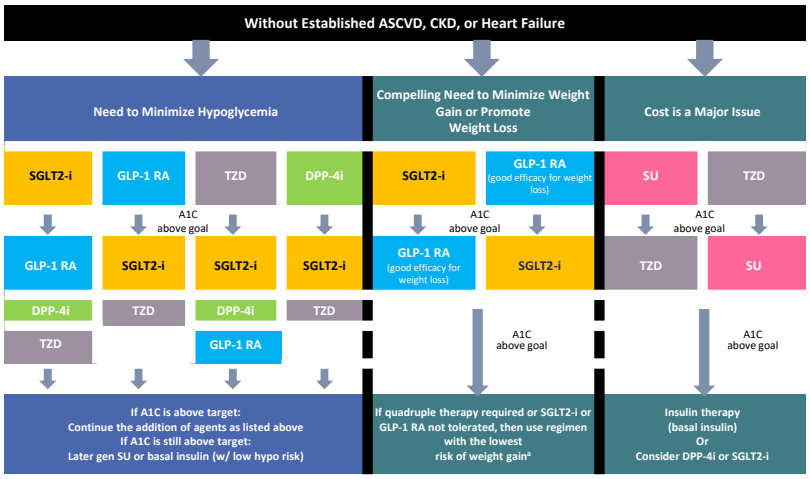


*Label indication of reducing CVD events

ADA = American Diabetes Association; ASCVD = atherosclerotic cardiovascular disease; CKD = chronic kidney disease; CVD = cardiovascular disease; ; eGFR = estimated glomerular filtration rate; HF = heart failure

Adapted from American Diabetes Association. Standards of Medical Care in Diabetes 2020. *Diabetes Care*. 2020;43(Supplement 1):S1-S212.

ADA 2020 Standards of Care Antihyperglycemic Medication in Type 2 Diabetes: Focus w/o ASCVD, CKD, or HF



Adapted from American Diabetes Association. Standards of Medical Care in Diabetes 2020. *Diabetes Care.* 2020;43(supplement 1):S1-S212.

[a]DPP-4i (if not on GLP-1 RA based on weight neutrality; if DPP-4i is not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of SU, TZD, or basal insulin.

ADA = American Diabetes Association; ASCVD = atherosclerotic cardiovascular disease; CKD = chronic kidney disease; DPP-4i = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1; HF = heart failure; RA = receptor agonist; SU = sulfonylurea; TZD = thiazolidinedione

ACC Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients with Type 2 Diabetes and Atherosclerotic Cardiovascular Disease

A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways
Endorsed by the American Diabetes Association

A Focus on Comprehensive CV Risk Reduction in T2D

- ACC created a roundtable with several experts in diverse medical specialties: cardiology, family medicine, internal medicine, and endocrinology, including physicians, nurses, advanced practice providers, and pharmacists
- Takeaways
  - Need for paradigm shift from focusing on glycemic control to more comprehensive focus on reducing CV risk and preventing CV death
  - Some emerging therapies proved to reduce CV death in patients with established CVD or at high-risk, and CV clinicians have a role in prescribing them
- SGLT2-inhibitors – 2 drugs demonstrated reduction in MACE and hHF, one also in CV death and ACM
- GLP-1 RAs – one drug demonstrated significant reduction in CV events

ACC = American College of Cardiology; ACM = all-cause mortality; CV = cardiovascular; CVD = cardiovascular disease; GLP-1 RAs = glucagon-like peptide-1 receptor agonists; hHF = hospitalization for heart failure; MACE = major adverse cardiovascular event
Das SR et al. *J Am Coll Cardiol.* 2018;72:3200-23.

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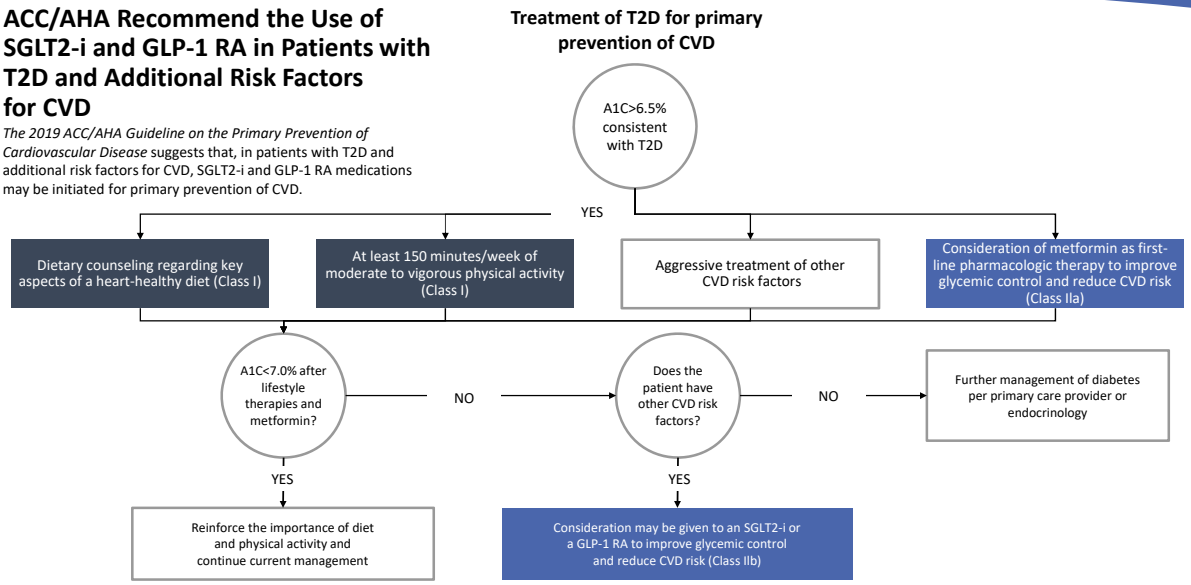
ACC/AHA Recommend the Use of SGLT2-i and GLP-1 RA in Patients with T2D and Additional Risk Factors for CVD

The 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease suggests that, in patients with T2D and additional risk factors for CVD, SGLT2-i and GLP-1 RA medications may be initiated for primary prevention of CVD.



ACC = American College of Cardiology; AHA = American Heart Association; GLP-1 RA = glucagon-like peptide-1 receptor agonist; A1C = glycated hemoglobin

Arnett DK et al. *Circulation.* 2019;140(11)e596-e646. doi:10.1161/CIR.0000000000000678.

AACE/ACE Algorithm

Management of Type 2 Diabetes: Putting the 2020 Guidelines into Practice

Principles of the AACE/ACE Comprehensive T2D Management Algorithm

1	Lifestyle medication underlies all therapy (e.g., weight control, physical activity, sleep, etc.)
2	Avoid hypoglycemia
3	Avoid weight gain
4	Indivi
5	**Optimal A1C is ≤6.5% or as close to normal as is safe and achievable**
6	Therapy choices are patient-centric based on A1C at presentation and shared decision-making
7	Choice of therapy reflects ASCVD, CHF, and renal status
8	Comorbidities must be managed for comprehensive care
9	Get to the goal as soon as possible – adjust at ≤3 months until at goal
10	Choice of therapy includes ease of use and affordability
11	CGM is highly recommended, as available, to assist patients in reaching goals safely

Glycemic Targets

A1C ≤ 6.5%: For patients without concurrent serious illness and at low hypoglycemia risk

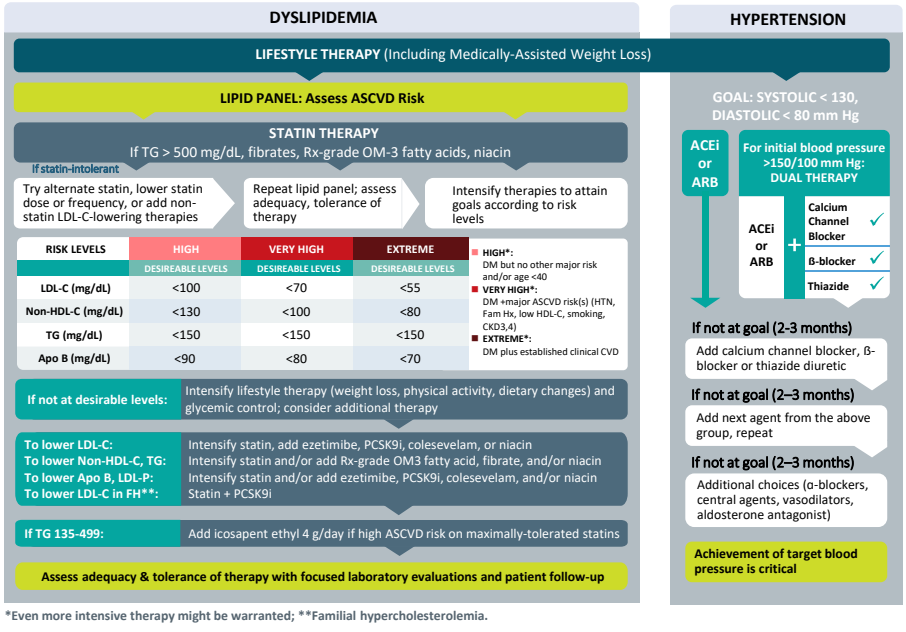
For patients with concurrent serious illness and at risk for hypoglycemia: A1C > 6.5%

Adjustments based on: Age, duration of diabetes, comorbid conditions, hypoglycemia risk, patient motivation, adherence, and life expectancy

A1C = glycated hemoglobin; AACE = American Association of Clinical Endocrinologists; ACE = American College of Endocrinology; ASCVD = atherosclerotic cardiovascular disease; CGM = continuous glucose monitoring; CHF = congestive heart failure

Garber AJ et al. *Endocr Pract*. 2020;26:107-39.

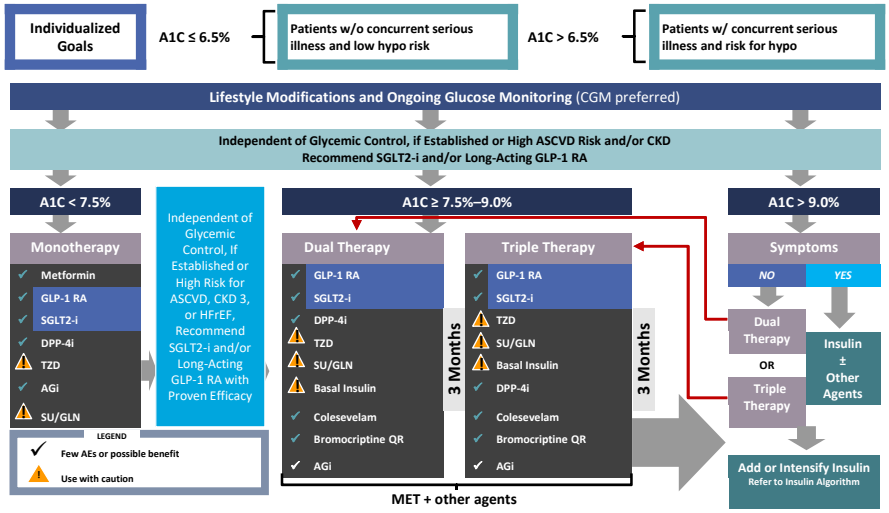
ASCVD Risk Factor Modifications Algorithm



*Even more intensive therapy might be warranted; **Familial hypercholesterolemia.

Management of Type 2 Diabetes: Putting the 2020 Guidelines into Practice

AACE/ACE 2020 Algorithm for Glycemic Management



A1C = glycated hemoglobin; AACE = American Association of Clinical Endocrinologists; ACE = American College of Endocrinology; AEs = adverse events; AGi = alpha-glucosidase inhibitor; ASCVD = atherosclerotic cardiovascular disease; CGM = continuous glucose monitoring; CHF = congestive heart failure; CKD = chronic kidney disease; DPP-4i = dipeptidyl peptidase-4 inhibitor; GLN = glinides; GLP-1 RA = glucagon-like peptide-1 receptor agonist; HFrEF = heart failure with reduced ejection fraction; SGLT2-i = sodium glucose cotransporter 2 inhibitor; SU = sulfonylurea; TZD = thiazolidinedione.
Adapted from Garber AJ et al. *Endocr Pract*. 2020;26:107-39.

By national T2D algorithms, if a patient has an A1C of 6.4% on metformin and sulfonylurea, a history of a myocardial infarct and heart failure (HFrEF), what, if any, further therapy would be recommended?

a. No further therapy, the patient is at A1C goal
b. A GLP-1 receptor agonist
c. An SGLT2 inhibitor
d. A thiazolidinedione (TZD)

Commonalities Between the Guidelines and Treatment Recommendations

An Early Proactive Approach to Management Is Advocated

ADA Standards of Medical Care[1]	Commonalities of Recommendations[1,2]	AACE/ACE Algorithm[2]
<7% for most, less/more stringent for others	Lifestyle modification and disease education are the foundation of the treatment plan	≤6.5% for most, customize for individual patients
Consider initial combination therapy when A1C is 1.5%–2.0% above goal	Individualize targets, achieving as low an A1C as is reasonable	Consider dual therapy when A1C ≥ 7.5%
Irrespective of A1C: if ASCVD, choose an agent with indication to reduce CVD events, if HF or CKD, choose an agent with proven efficacy	Assess target achievement every 3 months and intensify as necessary	Irrespective of A1C, in presence of established ASCVD or high-risk stage 3 CKD or HFrEF, choose agent with proven efficacy
Efficacy, hypoglycemia risk, impact on weight, potential side effects, renal effects, delivery method, cost, patient preferences	Treatment approach reflects ASCVD, HF, and renal status	Patient attributes, efficacy, tolerability, side effect profile, ease of use, cost, hypoglycemia risk, weight, MOA
Address BP, lipids, smoking cessation, weight, lifestyle	Additional considerations in patients without a CV or renal comorbidities	Address BP, lipids, smoking cessation, weight, lifestyle
	Comprehensive risk management beyond	

A1C = glycated hemoglobin; ADA = American Diabetes Association; AACE = American Association of Clinical Endocrinologists; ACE = American College of Endocrinology; ASCVD = atherosclerotic cardiovascular disease; BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; MOA = monoamine oxidase

1. American Diabetes Association. Standards of Medical Care in Diabetes 2020. *Diabetes Care*. 2020;43(supplement 1):S1-S212. 2. Garber AJ et al. *Endocr Pract*. 2020;26:107-39.

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Profiles of Antihyperglycemic Medications

	MET	GLP-1 RA	SGLT2-i	DPP-4i	AGi	TZD (moderate dose)	SU / GLN	COLSVL	BCR-QR	INSULIN	PRAML
HYPO	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate/Severe: Mild	Neutral	Neutral	Moderate to Severe	Neutral
WEIGHT	Sight Loss	Loss	Loss	Neutral	Neutral	Gain	Gain	Neutral	Neutral	Gain	Loss
RENAL/GU	Contraindicated if eGFR < 30 mL/min/1.73 m²	Exenatide Not Indicated CrCl < 30; Potential Benefit LA GLP-1 RA	Not Indicated for eGFR < 45 mL/min/1.73 m²; See #1; Genital Mycotic Infections; Potential CKD Benefit; See #1	Dose Adjustment Necessary (Except Linagliptin); Effective in Reducing Albuminuria	Neutral	Neutral	More Hypo Risk	Neutral	Neutral	More Hypo Risk	Neutral
GI Sx	Moderate	Moderate	Neutral	Neutral	Moderate	Neutral	Neutral	Mild	Moderate	Neutral	Moderate
CHF / CARDIAC / ASCVD	Neutral	Neutral; Potential Benefit LA GLP-1 RA	Prevent HF Hospitalization Manage HFrEF; See #2; See #3	See #4	Neutral	Moderate; May Reduce Stroke Risk	Neutral; Possible ASCVD Risk	Neutral; Lowers LDL-C	Neutral; Safe	CHF Risk; Neutral	Neutral
KETOACIDOSIS	Neutral	Neutral	DKA Can Occur in Various Stress Settings	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral

1. Canagliflozin indicated for eGFR >30 mL/min/1.73 m² in patients with CKD 3 + albuminuria.
2. Dapagliflozin – primary prevention of HF hospitalization and efficacy in HFrEF.
3. Empagliflozing – FDA approved to reduce CV mortality. Canagliflozin – FDA approved to reduce MACE events.
4. Possible increased hospitalization for heart failure with alogliptin and saxagliptin.

- Few adverse events or possible benefits
- Use with caution
- Likelihood of adverse effects

Cardiovascular Indications Among SGLT2 Inhibitors and GLP-1 Receptor Agonists

SGLT2 Inhibitors			GLP-1 Receptor Agonists		
empagliflozin[1]	canaglflozin[2]	dapagliflozin[3]	dulaglutide[4]	liraglutide[5]	semaglutide[6]
With CVD *(CV Death only)*	With CVD		With CVD or MRF	With CVD	With CVD
	With T2D and **albuminuria**	With T2D and **CVD or MRF**			
	With T2D and **albuminuria**	HFrEF **With And *Without T2D***		Adjunct to lifestyle modifications	

- To reduce the risk of **major adverse cardiovascular events** (MACE) in adults **with T2D**
- To reduce the risk of **hospitalization for heart failure** in adults **with T2D**
- To reduce the risk of **end-stage kidney disease**, **doubling of serum creatinine**, in adults **with T2D** and **diabetic nephropathy with albuminuria** (>300 mg/day).
- To reduce the risk of cardiovascular death and hospitalization for heart failure in adults with **heart failure with reduced ejection fraction** (NYHA class II–IV).
- Chronic **weight management** in adult patients with an initial BMI of **≥30 kg/m²** or **≥27 kg/m²** in the presence of at least **one weight-related** comorbid condition (e.g., **T2D**)

BMI = body mass index; CV = cardiovascular; CKD = chronic kidney disease; CVD = cardiovascular disease; GLP-1 = glucagon-like peptide-1; HFrEF = heart failure with reduced ejection fraction; MRF = multiple risk factors; NYHA = New York Heart Association; SGLT2-i = sodium glucose cotransporter 2

1. Jardiance [package insert]. Rhein, Germany: Boehringer Ingelheim; 2014. 2. Invokana [package insert]. Beerse, Belgium: Janssen; 2013. 3. Farxiga [package insert]. Cambridge, UK: AstraZeneca; 2014. 4. Trulicity [package insert]. Indianapolis, IN: Eli Lilly and Co; 2014. 5. Victoza [package insert] Bagsværd, Denmark: Novo Nordisk; 2010. 6. Ozempic [package insert]. Bagsværd, Denmark: Novo Nordisk; 2017.

Summary of Guidelines

- Guideline recommendations continue to focus on patient-centered glycemic management with individualized A1C target and choice of therapy based on numerous patient-specific factors
- Metformin and comprehensive lifestyle management remain the foundational therapy recommendations
- After metformin, choice of therapy should be based on ASCVD, HF, and renal status of the patient and prioritize minimizing weight gain and the risk of hypoglycemia
  - For patients with ASCVD, HF, or CKD, add either an SGLT2-i or GLP-1 RA with proven CVD benefit, regardless of baseline A1C or individualized A1C target
  - For patients without ASCVD, HF, or CKD, treatment should focus on the individual patient's needs and preferences, including weight, hypoglycemia, and cost concerns

A1C = glycated hemoglobin; ASCVD = atherosclerotic cardiovascular disease; CKD = chronic kidney disease; CVD = cardiovascular disease; HF = heart failure; GLP-1 RA = glucagon-like peptide-1 receptor agonist; SGLT2-i = sodium glucose cotransporter 2 inhibitor

Selected References

- American Diabetes Association. Pharmacologic approaches to glycemic control: standards of medical care in diabetes – 2020. *Diabetes Care*. 2020;43(suppl 1):S98-S110.
- Garber AJ et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm – 2020 Executive summary. *Endocr Pract*. 2020;26:107-39.
- Arnett DK et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. *Circulation.* 2019;140(11):e596-e646.